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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/509,533 | 05/26/2005 | David J. Waxman | 701586-52522 | 1019 |

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| EXAMINER | |
|---|---|
| NGUYEN, QUANG | |
| **ART UNIT** | **PAPER NUMBER** |
| 1633 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/509,533 | WAXMAN ET AL. | |
| | Examiner | Art Unit | |
| | Quang Nguyen, Ph.D. | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-36 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-36 are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-36 are pending in the present application, and they are subjected to the following restrictions.

### *Election/Restrictions*

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 2-18, 31-33, drawn to a method of prolonging expression of a heterologous gene encoding a prodrug activating enzyme; and a method of increasing the concentration of a chemotherapeutic drug in or in the vicinity of a target cell in a mammal.

Group II, claims 20, 22, 25-26, 34 and 35, drawn to a method of prolonging expression of a heterologous gene encoding a therapeutic factor having antiangiogic activity; and a method of increasing the concentration of the same therapeutic factor in a mammal.

Group III, claims 20, 22, 25-26, 34 and 35, drawn to a method of prolonging expression of a heterologous gene encoding a therapeutic factor having cyotoxic activity; and a method of increasing the concentration of the same therapeutic factor in a mammal.

Group IV, claims 20, 22, 25-26, 34 and 35, drawn to a method of prolonging expression of a heterologous gene encoding a therapeutic factor having immune modulatory activity; and a method of increasing the concentration of the same therapeutic factor in a mammal.

Claims 1, 19, 21, 23-24, 27-30 and 36 link a plurality of different inventions of Groups I-V using different heterologous genes having different structures and different

chemical properties one from the others. For example, a heterologous gene encoding a prodrug activating enzyme of Group I is different from a heterologous gene encoding a therapeutic factor having anti-angiogenic activity or cytotoxic activity or immunomodulatory activity in Groups II-IV, respectively.

Upon the allowance of the linking claims, the restriction requirement as to the linked invention shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims or the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-132(CCPA 1971). See also MPEP 804.01.

The technical feature linking Groups I-IV appears to be that a cell is transduced with both a vector encoding a heterologous gene and a vector encoding an apoptosis inhibiting agent.

However at the effective filing date of the present application (3/25/02), at least Luo et al (Human Gene Therapy 12:2191-2202, 2001; IDS) already taught a method for co-expression of p34 in FasL-transduced vascular smooth muscle (VSM) cells *in vivo* using Ad2/FasL/p35 to promote their survival and enhance FasL-induced apoptosis of

adjacent VSM cells, and thereby facilitate a greater inhibition of neointimal formation (see at least the abstract).

Therefore, the technical feature linking the inventions of Groups I-IV does not constitute a special technical feature a defined by PCT Rule 13.2, as it does not differentiate the claimed subject matter a whole over the prior art. Since according to Rule 13.2 PCT the presence of such a common or corresponding special technical feature is an absolute prerequisite for unity to be established, and given that there does not appear to be any other technical feature common to the claimed subject matter as a whole which might be able to fulfill this role, the currently claimed subject matter lacks unity of invention according to Rule 13.1 PCT.

Consequently, the claimed subject matter is restricted into the above Groups of Inventions for the following reasons.

The currently claimed subject matter (Inventions of Groups I-IV) lacks unity of invention according to Rule 13.1 PCT for the following reasons.

The methods in Groups I-IV are directed to different methods using different heterologous genes that do not share the same common structures and they have different properties one from the others. For example, the method of Group I is directed to a method of prolonging expressing of a heterologous gene encoding a prodrug activating enzyme; the method of Group II is drawn to a method of prolonging expressing of a heterologous gene encoding a therapeutic factor having anti-angiogenic activity; the method of Group III is directed to a method of prolonging expressing of a heterologous gene encoding a therapeutic factor having cytotoxic activity; and the

method of Group IV is drawn to a method of prolonging expressing of a heterologous gene encoding a therapeutic factor having immune modulatory activity.

Because the currently claimed subject matter lacks unity according to Rule 13.1 PCT for the reasons set forth above, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

***Species restriction:***

**A. Should Applicants elect Group I**, this application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

1. ***A single species of apoptosis inhibiting agent recited in either claim 6 or claim 28.***
2. ***A single species of a prodrug-activating enzyme recited in the Markush group of claim 7.***

***Should Applicant elect the prodrug-activating cytochrome P450 enzyme, please further elect a single species of the prodrug-***

***activating cytochrome P45 enzyme recited in the Markush group of claim 10.***

3. ***A single species of a prodrug recited in the Markush group of claim 8.***
4. ***A single species of a factor promoting apoptosis recited in the Markush group of claim 16.***
5. ***A single species of a death receptor ligand recited in the Markush group of claim 18.***

**B. Should Applicants elect any one of the Groups II-IV**, this application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

1. ***A single species of a therapeutic factor having anti-angiogenic or cytotoxic or immune modulatory activity recited in the Markush group of either claim 22 or claim 26.***
2. ***A single species of apoptosis inhibiting agent recited in claim 28.***

**Applicant is required, in reply to this action,** to elect a single species consistent to the elected invention **to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the**

**claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.**

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

1. Each of the listed species of an apoptosis inhibiting agent in A1 is different structurally and chemically one from the others.

2. Each of the listed species of a prodrug-activating enzyme in A2 is different structurally and chemically one from the others.

3. Each of the listed species of a prodrug in A3 is different structurally and chemically one from the others.

4. Each of the listed species of a factor promoting apoptosis in A4 is different structurally and chemically one from the others.

5. Each of the listed species of a death receptor ligand in A5 is different structurally and chemically one from the others.

6. Each of the listed species of a therapeutic factor having anti-angiogenic, cytotoxic or immune modulatory activity in B1 is different structurally and chemically one from the others.

7. Each of the listed species of an apoptosis inhibiting agent in B2 is different structurally and chemically one from the others.

Each of the aforementioned species is different structurally one from the others. Each different structure can be considered to be a "special technical feature"; and therefore the listed species lack the same or corresponding special technical features.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

**To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.**

**Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.**

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

QUANG NGUYEN, PH.D.
PRIMARY EXAMINER